TUMOR ASSOCIATED ANTIGEN PEPTIDES AND USE OF SAME AS ANTI-TUMOR VACCINES

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FIELD AND BACKGROUND OF THE INVENTION

The present invention relates to tumor associated antigen (TAA) peptides and to the use of same, of polynucleotides encoding same and of cells presenting same as anti-tumor vaccines. More particularly, the present invention relates to tumor associated antigen peptides derived from Uroplakin Ia, Ib, II and III, Prostate specific antigen (PSA), Prostate acid phosphatase (PAP) and Prostate specific membrane antigen (PSMA), BA-46 (Lactadherin), Mucin (MUC-1), and Teratocarcinoma-derived growth factor (CRIPTO-1) and the use of same as anti-tumor vaccines to prevent or cure bladder, prostate, breast or other cancers, carcinomas in particular. Most particularly, the present invention relates to tumor associated antigen peptides which are presentable to the immune system by HLA-A2 molecules.

Local therapy such as surgical excision or ablation by radiation is a mainstay for the treatment of primary cancer and is curative for a percentage of patients. However, many malignancies will recur locally or at a distant site. Thus the prevention or cure of metastases remains a major focus in clinical oncology (1). Although early detection followed by surgery provides good prognosis for a number of major cancer types, a large fraction of patients would need adjuvant therapy. Part of these patients will, with time, succumb to metastasis (2-4). Alternative approaches based on gene therapy and immunotherapy have been the focus of attention in the last years. One such approach is specific active immunotherapy (SAI, 5). The objective of SAI is to stimulate a tumor specific cytotoxic T lymphocytes (CTL) immune response that is capable of eliminating residual metastatic disease and induce a state of immunity to protect the patients from recurrent disease. The underlying assumption of SAI is that tumor cells express tumor antigens which are sufficiently distinct in structure or context to induce an effective CTL response (6). Although the validity of these assumptions was questioned, a number of studies in the last decade have demonstrated the rational of SAI. In a landmark study, van Pel and Boon have shown that tumor associated antigens (TAAs) can be isolated and defined (7). Importantly, *ex-vivo* manipulations of "non-immunogenic" animal tumor cells can be used to elicit effective immune responses which will also recognize parental "non-immunogenic" tumor cells (8). Studies employing rodent tumor models with little intrinsic immunogenicity have shown that genetically modified tumor cells transduced to express MHC class I, cytokines such as IL-1, IL-2, IL-4, IL-6, IL-7, IL-12, IFN or GM-CSF or costimulatory molecules such as B7-1 or B7-2 were